1991

Self-Activation and Inhibition: A Simple Nonlinear Model

J. A. Adam
Old Dominion University, jadam@odu.edu

Original Publication Citation

Adam, J. A. (1991). Self-activation and inhibition: A simple nonlinear model. *Applied Mathematics Letters, 4*(2), 85-87. doi:10.1016/0893-9659(91)90175-u

Appl. Math. Lett. Vol. 4, No. 2, pp. 85–87, 1991
Printed in Great Britain.

0893-9659/91 $3.00 + 0.00

Self-Activation and Inhibition: A Simple Nonlinear Model

JOHN A. ADAM

Department of Mathematics and Statistics
Old Dominion University

(Received August 1990)

Abstract. Self-activation and self-inhibition of cell number density (or growth factor concentration) due to a spatially localized source are studied. Both the time-independent and time-dependent models are examined, and the linear stability of the resulting three steady states of the former is discussed.

Recent experimental studies on tumor growth factors (TGF) indicate [1], among other things, that TGF's are multifunctional, i.e., they can have both stimulatory and inhibitory effects on cell division and other cell processes (depending on concentration) and different effects on different cells. Specifically, at low to intermediate TGF concentration, mitotic activity can be stimulated; inhibited at higher concentration, and TGF is highly toxic to cells at still higher concentrations. In the following simple model we consider the number density $c(x,t)$ of normal but otherwise unspecified cells subject to depletion rate γ with diffusion away from a localized site of number density production at $x = 0$. The form of this source term is based on the above properties of TGF (see Figure 1(a)). The model is sufficiently general to allow $c(x,t)$ to represent the concentration of TGF also, with γ in that situation being a decay coefficient. The governing equation is

$$\frac{\partial c}{\partial t} + \gamma c - D\frac{\partial^2 c}{\partial x^2} = \lambda f(c)\,\delta(x), \qquad -\infty < x < \infty, \tag{1}$$

D being a diffusion coefficient and λ being a production rate. The steady state equation

$$\frac{d^2 c}{dx^2} - \alpha^2 c = -\frac{\lambda}{D} f(c)\,\delta(x) = S(x), \tag{2}$$

has the unique solution

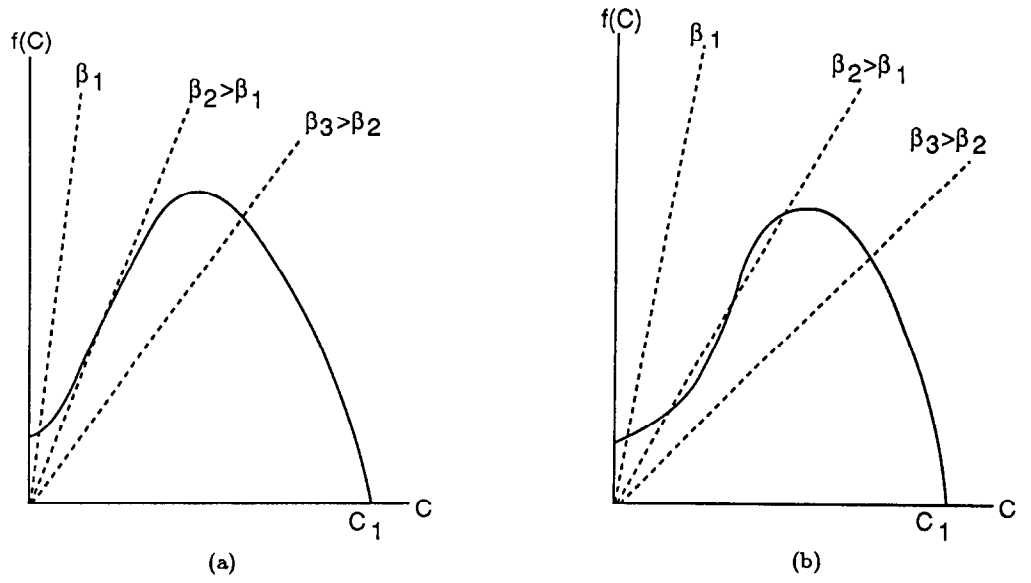
$$c(x) = \int_{-\infty}^{\infty} G(x,x')\,S(x')\,dx', \tag{3}$$

where

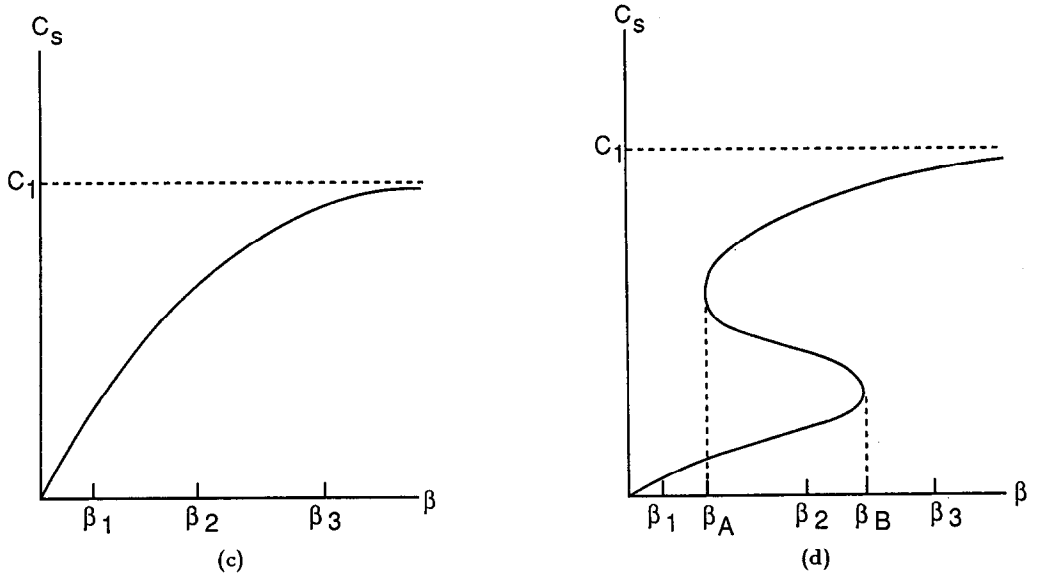
$$G(x,x') = -\frac{1}{2\alpha} e^{-\alpha|x-x'|} \tag{4}$$

and $\alpha^2 = \gamma/D$.

I am very grateful to Dr. David Axelrod for his correspondence about growth factors and their importance in cell biology.



Graphical representation of solutions of the equation $c/\beta = f(c)$.



Location of steady state solutions c_s, as a function of β, for 1(a) and 1(b), respectively.

Figure 1.

Hence,

$$c(x) = \left(\frac{\lambda}{2\alpha D}\right) e^{-\alpha|x|} f(c(0)), \tag{5}$$

or, at x=0,

$$y = c(0) = \beta f(y), \tag{6}$$

where β is obviously defined from (5). Figures 1(a) and 1(b) indicate that three steady states will exist if and only if, for $f(0) > 0$,

$$\beta f'(c_s) > 1, \tag{7}$$

where c_s is a fixed point of the mapping $\theta(y) = \beta f(y)$. Otherwise, there is a unique steady state (Figure 1(c)). The bifurcation points for the former are indicated in Figure 1(d)). The

linear stability of each c_s may be investigated via Laplace transformation. Let

$$c(x,t) = c_0(x) + \epsilon(x,t), \tag{8}$$

where $\epsilon(x,t)$ has transform $\tilde{\epsilon}(x,s)$, and

$$\epsilon(x,t) = \frac{1}{2\pi i}\int_{\xi-i\infty}^{\xi+i\infty} e^{st}\,\tilde{\epsilon}(x,s)\,ds, \tag{9}$$

and $\xi > \mathrm{Re}(s_0)$, s_0 being the pole of $\tilde{\epsilon}(x,s)$ with the largest real part. The solution of equation (1) is given by

$$c(x,t) = \int_{-\infty}^{\infty} c(x',0)\,G(x,x',t,0)\,dx' + \lambda\int_0^t f(c(0,t'))\,G(x,0,t,t')\,dt', \tag{10}$$

where

$$\sqrt{4\pi D(t-t')}\,G(x,x',t,t') = \exp\left[-\left(\frac{(x-x')^2}{4D(t-t')} + \gamma(t-t')\right)\right]. \tag{11}$$

Linearizing $f(c)$ about the steady state value $c_0(0)$ (by (5), $c(x)$ is simply related to $c(0)$),

$$f(c(0,t)) = f(c_0(0)) + m\,\epsilon(0,t), \tag{12}$$

where

$$m = f'(c)\Big|_{c_0(0)}.$$

Hence,

$$\epsilon(0,t) = \int_{-\infty}^{\infty} G(0,x',t)\,\epsilon(x',0)\,dx' + \lambda m\int_0^t G(0,t-t')\,\epsilon(0,t')\,dt', \tag{13}$$

and using the convolution theorem, we find

$$\tilde{\epsilon}(0,s) = \frac{\tilde{g}(0,s)}{\{1-\lambda m\tilde{G}(0,s)\}}, \tag{14}$$

where $\tilde{G}(0,s) = \{2\sqrt{D(s+\gamma)}\}^{-1}$, and where $\tilde{g}(0,s)$ is the Laplace transform of the first term in equation (13). It is readily shown that $\tilde{g}(0,s)$ possesses no singularities for $\mathrm{Re}(s) > 0$, so stability is determined by the zeros of the denominator in equation (14). The condition for instability ($\mathrm{Re}(s) > 0$) is

$$\lambda\,|m| > 2\sqrt{D\gamma}. \tag{15}$$

For $m > 0$ this is just condition (7) for the existence of three steady states. It follows that the central branch $\beta_A - \beta_B$ corresponds to an unstable steady state, the other two being stable. If $m < 0$, and $\beta\,|m| > 1$, the steady state is unstable, and stable if $\beta\,|m| < 1$.

A similar type of analysis can be used in the study of spatial switching in coupled chemical systems [2].

References

1. M.B. Sporn and A.B. Roberts, Peptide growth factors are multifunctional, *Nature* **332**, 217 (1988).
2. R.M. Shymko and L. Glass, Spatial switching in chemical reactions with heterogeneous catalysis, *J. Chem. Phys.* **60**, 835 (1974).

Department of Mathematics and Statistics, Old Dominion University, Norfolk, Virginia 23529.